REMARKS

The invention relates to apparatus for performing liquid chromatography, which involves flow of a liquid carrying a sample, called the mobile phase, through a porous media, called a stationary phase. Different compounds in the sample will have differing rates of migration through the media, which causes the separation of the components in the subject sample. Liquid chromatography is commonly performed with reusable columns or with disposable cartridges, both of which are usually cylindrical, in which the media bed, typically resin beads, is bounded axially by porous plates, or plates containing defined flow paths, through which the mobile phase will flow into and from the media bed. Voids in the bed of stationary phase resin beads that may have resulted during shipping and other nonuniform packing conditions can deleteriously affect the operation of chromatography column and the accuracy of results.

More recently, a different type of stationary phase, called a "monolith," has been introduced. In this type of stationary phase, the polymer separation media is provided as a porous unitary structure, which can be formed inside a column by polymerizing the material inside a column, or can be preformed and then inserted into a column. Because the stationary phase is provided as unitary structure, it will not suffer from the shifting of individual particles as can happen with the resin beads.

The invention, as claimed in independent claim 1, relates to a disposable chromatography cartridge that contains a monolith chromatography stationary phase inside a vessel that has a flexible wall that is deformable by externally applied force so as to reduce the volume within the vessel. The application of external force and deformation of the flexible wall advantageously and unexpectedly provide for improved separation of the chemical compound passing through the monolith chromatography stationary phase. It is believed that the external force tends to close channels that may otherwise exist between the outside of the stationary phase and the inside of the wall and which otherwise may present low pressure by-pass channels. The external force may also tend to provide for more uniform flow through the stationary phase by closing voids therein. This improved performance is unexpected for the monolith stationary phase, because the monolith stationary phase does not have the problem of shifting of resin beads that is

known to occur with typical media, such that improved uniformity is expected for use of a deformable wall cartridge with the resin beads but not for the monoliths.

Claim 1 stands rejected as anticipated by or obvious over Frechet U.S. Patent No. 5,334,310. The examiner points to three passages for purported anticipatory disclosure of a monolith in a "flexible" tube.

The first passage noted in the office action is at col. 4, lines 29-30; this passage, however, refers to substantial rigidity and, if anything, is more of a teaching away then a teaching of the invention.

The second passage noted in the office action is at col. 2, lines 43-52 and the third is at col. 12, lines 6-19. The second passage describes teachings from a prior art Dutch patent application, and the third describes a duplication of the manufacture of the device described in the Dutch patent application. The passage at col. 2, lines 43-52 reads as follows:

> Dutch patent application No. 6,803,739 discloses the copolymerization of a solution of ethylene glycol bismethacrylate and ethylene glycol monomethacrylate in benzene in a flexible polytetrafluoroethylene tube. After polymerization, the benzene is removed and replaced by ethylene glycol monomethyl ether. The filled column that was obtained was used for gas-liquid chromatography. The column needs to be filled with ethylene glycol monomethyl ether in order to separate compounds in a gas-liquid chromatographic operation.

This passage thus relates to gas-liquid chromatography, not liquid chromatography as claimed. In fact, the introduction of gas into a liquid chromatography apparatus, as described in the invention, can significantly degrade the performance of the separation. Also, claim 1 herein recites "a flexible wall that is deformable by externally applied force so as to reduce a volume within said vessel." While Frechet mentions a flexible tube, it does not mention being deformable by externally applied force, and does not disclose this claim feature under principles of inherency, as a flexible tube might include other structure preventing it from being deformable by externally applied force.

The third passage, at col. 12, lines 8-20, reported that the device described in the Dutch application did not work:

> COMPARATIVE EXAMPLE A
>
> The procedure of Example 1 is repeated except that the polymerization mixture is replaced by the formulation of Dutch patent application No. 6,803,739, example II, the tube is of flexible polytetrafluoroethylene, and the polymerization temperature is 60.degree. C. When the resulting tube and with its polymer plug is connected to a conventional chromatograph, essentially no flow of tetrahydrofuran through the plug is observed at pressures as high as 40 MPa (6,000 psi). When the plug is evaluated for pore size distribution as in Example 6 by cutting the tube apart to remove the plug, no pores larger than about 200 nm are found.

The third passage thus is also deficient for the same reasons mentioned above for the second passage, namely the discussion in this passage relates to gas-liquid chromatagraphy, not liquid chromatography as claimed, and there is no mention being deformable by externally applied force.

Moreover, the fact that the device described in the second and third paragraphs relied upon in the Office Action does not work (as described in Frechet itself) makes it clear that the discussion in both the second and third passages is not enabling, and therefore, these passages are not useful as prior art references.

The law requiring that a reference must be enabling in order for it to be a valid anticipatory reference is clear. The Federal Circuit has repeated this principle many times. For example:

> It is well settled that prior art under 35 U.S.C. §102(b) must sufficiently describe the claimed invention to have placed the public in possession of it. Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his own knowledge to make the

> claimed invention. Accordingly, even if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it was not enabling. [emphasis added] In Re Donohue, 766 F.2d 531, 533 (Fed. Cir. 1985).

In another case, the court wrote:

> A rejection for anticipation under section 102 requires that each and every limitation of the claimed invention be disclosed in a single prior art reference. In addition, the reference must be enabling and describe the applicant's claimed invention sufficiently to have placed it in the possession of a person of ordinary skill in the field of the invention. [emphasis added] In Re Paulsen, 30 F.3d 1475, 1478 (Fed. Cir. 1994).

This requirement is most often stated in connection with the technical arts that are viewed as being unpredictable, e.g. chemical cases. It is not, however, limited to only to chemical cases or to the unpredictable arts. As indicated by another more recent Federal Circuit court decision, Halifix Ltd. v. Blok-Lok, Ltd., 208 F.3d 1339, 1347 (Fed. Cir. 2000), it also applies to the mechanical arts. Halifax involved a method for securing two or more wythes (i.e., layers of masonry) is particularly instructive. The claimed invention, which was owned by Halifix Ltd., involved dry fixing or tying one masonry layer to another masonry structure. The single method claim included twelve elements among which were three that related to the operation of a tool that was needed to effect the anchoring of a tie into one of the masonry layers without creating any stress such as might be caused by hammering the tie into place.

Halifix brought a suit against Blok-Lok, Ltd. alleging that the company was infringing its patent. Blok-Lok defended by arguing that the patent was invalid because Halifix had disclosed the invention in a brochure which Halifix had distributed to the public in 1993, which was more than one year prior to filing its patent application. The 1993 brochure described Halifix stainless steel ties and their use in masonry refacing and new construction and it described the use of the ties in both "DryFix" and "Dry-Chemical Fix" methods of construction.

Halifix acknowledged that the brochure taught nine elements of the claim but argued that the three elements which related to how the tool operated were not taught. The court noted that:

> The brochure might nevertheless be anticipating if a person of ordinary skill in the art would understand the brochure as disclosing elements (8)-(10) and if such a person could have combined the brochure's description of the invention with his

> own knowledge to make the claimed invention. Halifix Ltd. v. Blok-Lok, Ltd., 208 F.3d 1339, 1347 (Fed. Cir. 2000)

Halifix argued that the tool required to perform the missing steps was not available at the time that the brochure was made public. Blok-Lok failed to submit any evidence that such a tool was available or that a person skilled in the art would know how to make one in view of the 1993 brochure. The court decided that the 1993 brochure did not anticipate the method claim and stated:

> We conclude, on the record before us, that Blok-Lok failed to provide clear and convincing evidence that the '93 brochure enables a person of ordinary skill in the art to practice the claimed method. In particular, Blok-Lok did not present any evidence indicating that a person of ordinary skill in the art could have made or obtained a tool capable of being used in the claimed method without an undue amount of experimentation. Halifix, supra, 208 F.3d at 1348.

In our case, the Frechet reference indicates that they tried to make the device and that it did not work, which is evidence that the description in Frechet in these passages is not enabling.

Thus, with respect to the rejection on Frechet, it is submitted that the reference is nonenabling, and that it does not teach or render the claimed invention obvious.

Claim 1 is also rejected as obvious over each of Leavesley U.S. Patent No. 5,601,708, McDonald U.S. Patent No. 4,250,035 and Conroy WO 97/43024 in view of Frechet or Hatch.

The first three references are said to disclose a vessel with a flexible wall, and the last two are cited for disclosure of monoliths. The first three references nowhere disclose or suggest the use of monoliths, and the last two nowhere disclose the use of a vessel with a flexible wall. There is no motivation to combine the teachings of these references. In particular, because the monolith beds do not suffer from the known problem of shifting that occurs in beds with resin beads, it would not be expected that the monolith beds would obtain improved uniformity with a deformable wall cartridge the way that the resin beads do.

In the office action it is asserted that advantages of using a monolith of compactness, high permeability, high column efficiency, ease of manufacture, lack of bed shifting, and better resolution noted in the secondary references Frechet and Hatch would motivate someone to use

them in the primary references. Applicants submit that the teachings in Frechet and Hatch do not suggest modifying the other references or using flexible cartridges as opposed to rigid cartridges. For example, the lack of bed shifting noted in the office action is a reason why one would not see any point in using a deformable cartridge for a monolith.

The references, taken alone or in combination, nowhere suggest the combination claimed in claim 1, and claim 1 is patentable under 35 USC 103(a) over these references.

The remaining claims depend on claim 1 and are allowable with it.

Applicant : Stephen E. Allen et al.
Serial No. : 09/855,155
Filed : May 14, 2001
Page : 11 of 11

Attorney's Docket No.: 15845-004001

Please apply the $205 fee for the Two-Month Extension of Time and any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: Sept 29, 2003

William E. Booth
Reg. No. 28,933

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906
20731972.doc